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# Lipase-catalyzed ring opening copolymerization of $\epsilon$ -caprolactone and $\beta$ -lactam

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## Percent yield calculation:

Reaction:  $\epsilon$ -CL +  $\beta$ -lactam  $\rightarrow$  copolymer + poly( $\epsilon$ -CL) + poly( $\beta$ -lactam)

## For 1:1 ratio of $\epsilon$ -CL and $\beta$ -lactam

mol  $\epsilon$ -CL = mol  $\beta$ -lactam = 1.4 mmol

Due to 1:1, ratio mol repeating unit of copolymer = 1.4 mmol

Theoretical yield of copolymer = mol of repeating unit  $\times$  molar mass of repeating unit

Theoretical yield of copolymer =  $1.4 \times 10^{-3}$  mol  $\times$  185.12 g/mol = 0.2592 gram

Yield (%) = (actual yield/theoretical yield)  $\times$  100%

Yield (%) from experiment 1 =  $(0.1388/0.2592) \times 100\% = 53\%$

Yield (%) from experiment 2 =  $(0.1228/0.2592) \times 100\% = 47\%$

**Average yield (%) from duplicate experiments =  $(53\% + 47\%)/2 = 50\%$**

**For 1:3 or 3:1 ratio of  $\epsilon$ -CL: $\beta$ -lactam**

**a. For 1:3**

$$\text{mol } \epsilon\text{-CL} = 0.7 \text{ mmol}$$

$$\text{mol } \beta\text{-lactam} = 2.1 \text{ mmol}$$

$\epsilon$ -CL act as limiting reagent, therefore mol repeating unit = mol  $\epsilon$ -CL = 0.7 mmol

$$\text{Theoretical yield} = 0.7 \times 10^{-3} \text{ mol} \times 185.12 \text{ g/mol} = 0.1296 \text{ gram}$$

$$\text{Yield (\%)} \text{ from experiment 1} = (0.0175/0.1296) \times 100\% = 13.5\%$$

$$\text{Yield (\%)} \text{ from experiment 2} = (0.0140/0.1296) \times 100\% = 10.8\%$$

$$\text{Average yield (\%)} \text{ from duplicate experiments} = (13.5\% + 10.8\%)/2 = 12.1\%$$

**b. For 3:1:**

$$\text{mol } \epsilon\text{-CL} = 2.1 \text{ mmol}$$

$$\text{mol } \beta\text{-lactam} = 0.7 \text{ mmol}$$

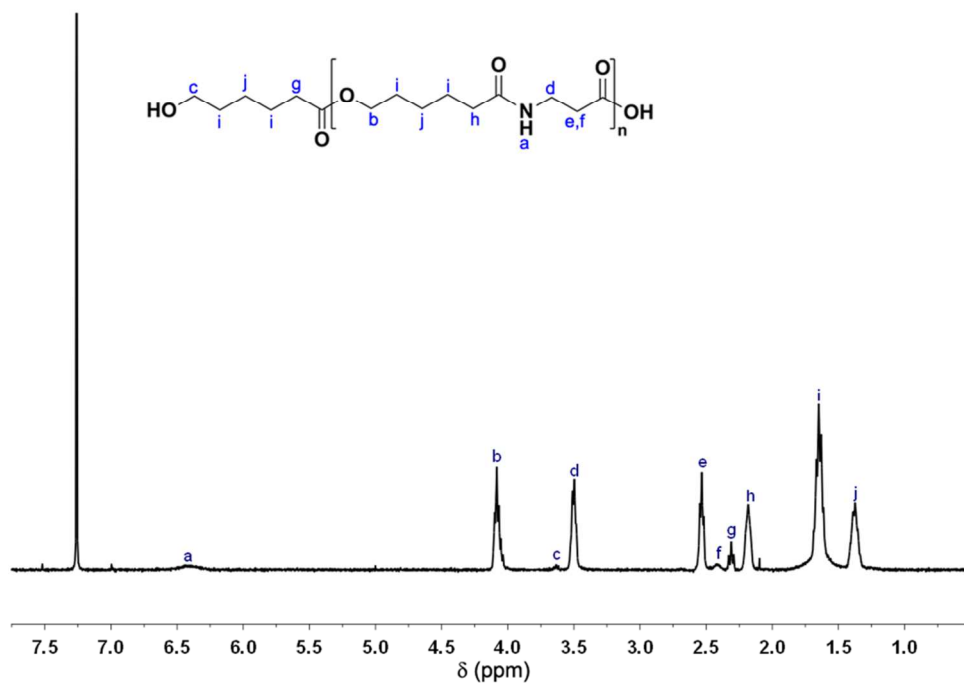
$\beta$ -lactam act as limiting reagent, therefore mol repeating unit = mol  $\beta$ -lactam = 0.7 mmol

$$\text{Theoretical yield} = 0.7 \times 10^{-3} \text{ mol} \times 185.12 \text{ g/mol} = 0.1296 \text{ gram}$$

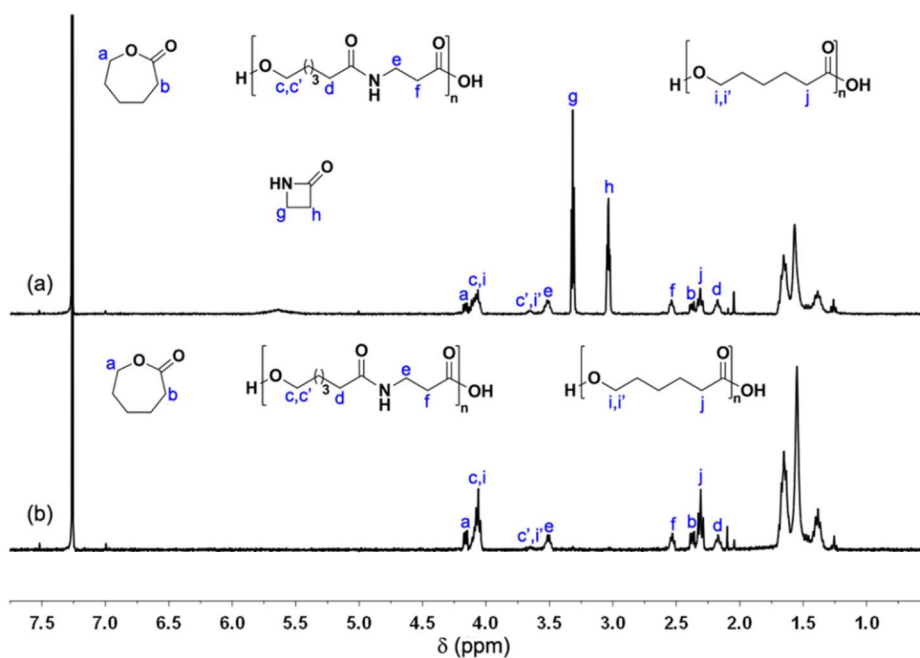
$$\text{Yield from experiment 1 (\%)} = (0.0625/0.1296) \times 100\% = 48\%$$

$$\text{Yield from experiment 2 (\%)} = (0.0519/0.1296) \times 100\% = 40\%$$

$$\text{Average yield (\%)} \text{ from duplicate experiments} = (48\% + 40\%)/2 = 44\%$$

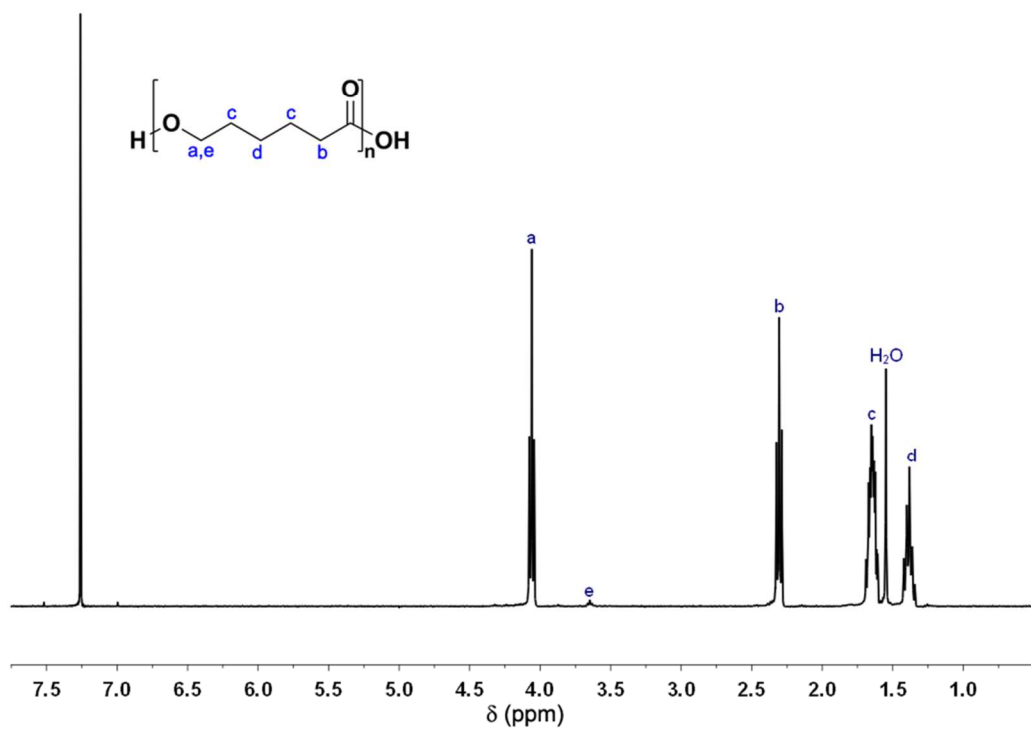


**Figure S1.**  $^1\text{H}$  NMR spectrum of poly( $\epsilon$ -CL-*co*- $\beta$ -lactam) in  $\text{CDCl}_3$

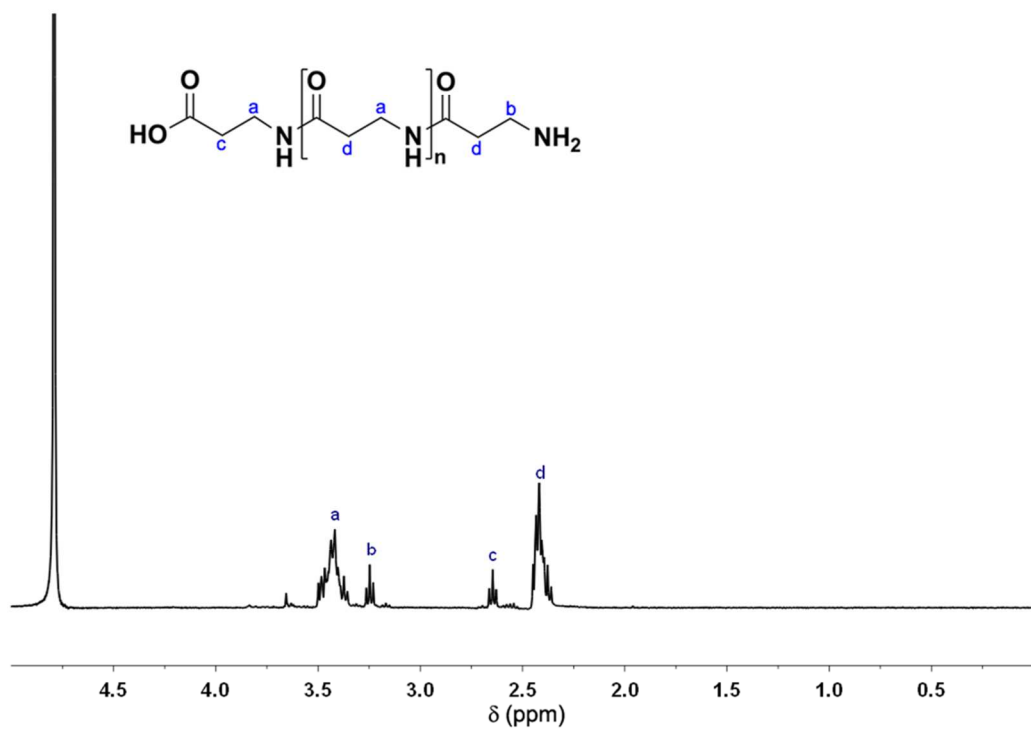


**Figure S2.**  $^1\text{H}$  NMR of the evaporated ethyl acetate fraction from the ring opening polymerization of  $\epsilon$ -CL and  $\beta$ -lactam in different feed ratios of  $\epsilon$ -CL: $\beta$ -lactam (a) 25:75 and (b)

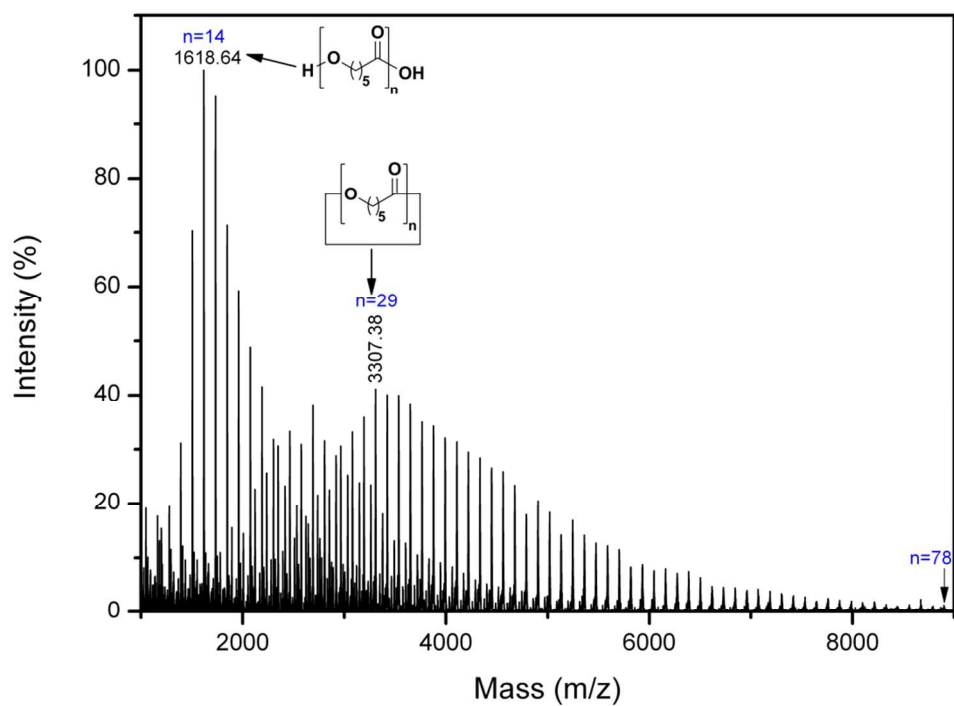
75:25



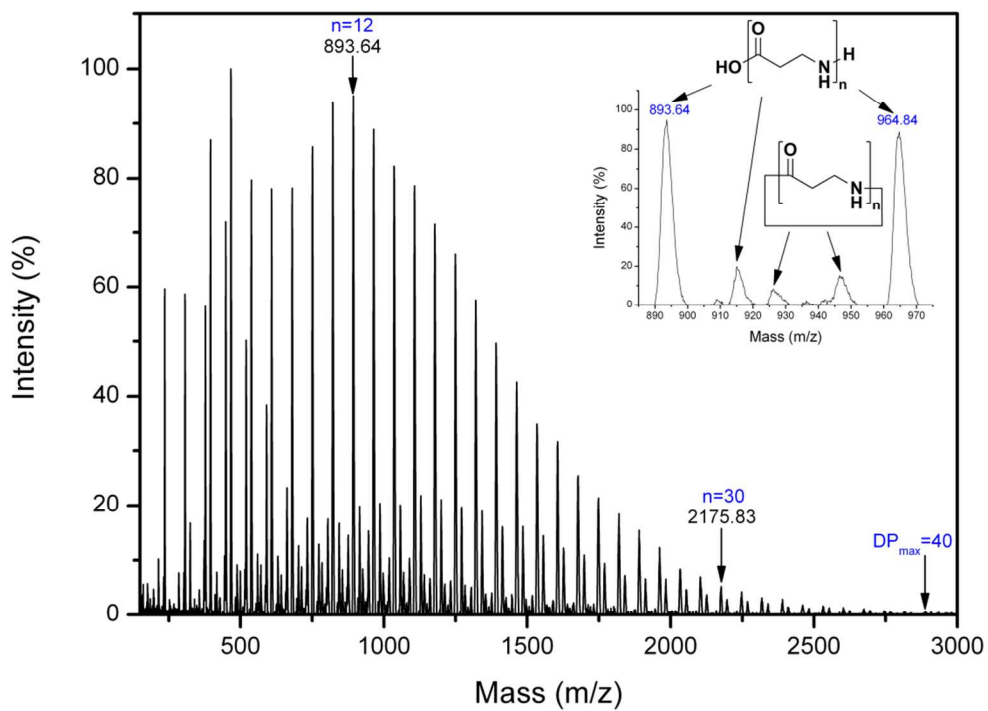
**Figure S3.**  $^1\text{H}$  NMR spectrum of poly( $\epsilon$ -caprolactone) in  $\text{CDCl}_3$



**Figure S4.**  $^1\text{H}$  NMR spectrum of poly( $\beta$ -lactam) in  $\text{D}_2\text{O}$



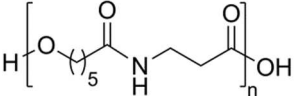

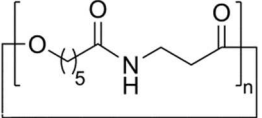

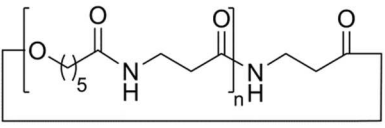

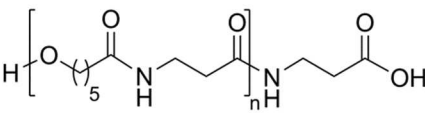

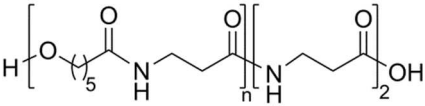

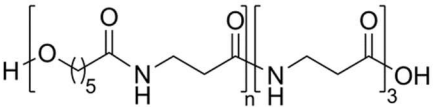

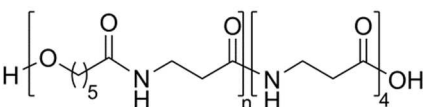

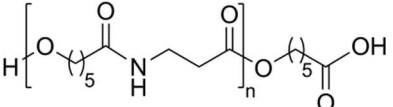

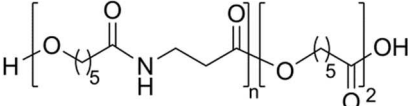


**Figure S5.** MALDI-ToF spectrum of poly( $\epsilon$ -caprolactone)



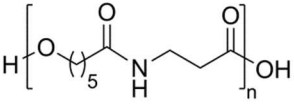

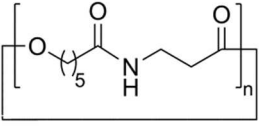

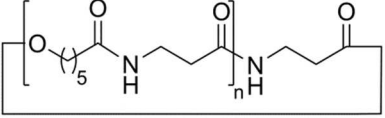


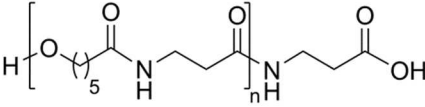


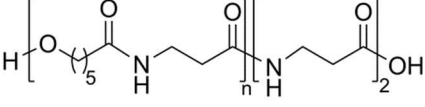


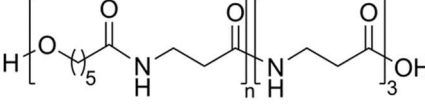

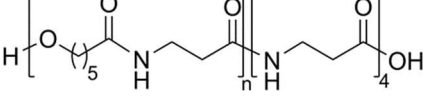

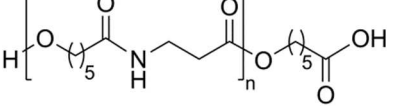

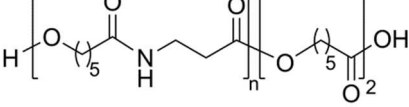


**Figure S6.** MALDI-ToF spectrum of poly( $\beta$ -lactam)

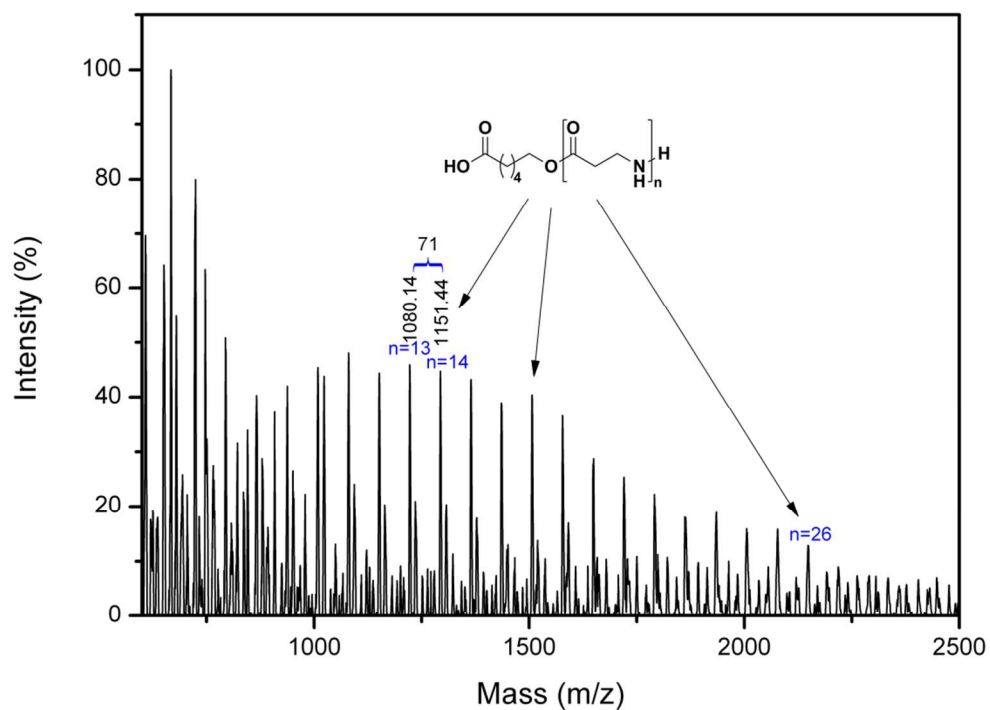
**Table S1.** Structures of poly( $\epsilon$ -CL-*co*- $\beta$ -lactam) resulted from the reaction with feed ratio 50:50 of  $\epsilon$ -CL: $\beta$ -lactam.

Symbol adduct	Structures	Mass of end group (amu)
$H^+$ :  $Na^+$ : 		18
$H^+$ : 		0
$H^+$ : 		71
$H^+$ : 		89
$H^+$ : 		160
$H^+$ : 		231.1
$H^+$ : 		302.2
$H^+$ : 		132.1
$H^+$ : 		246.1

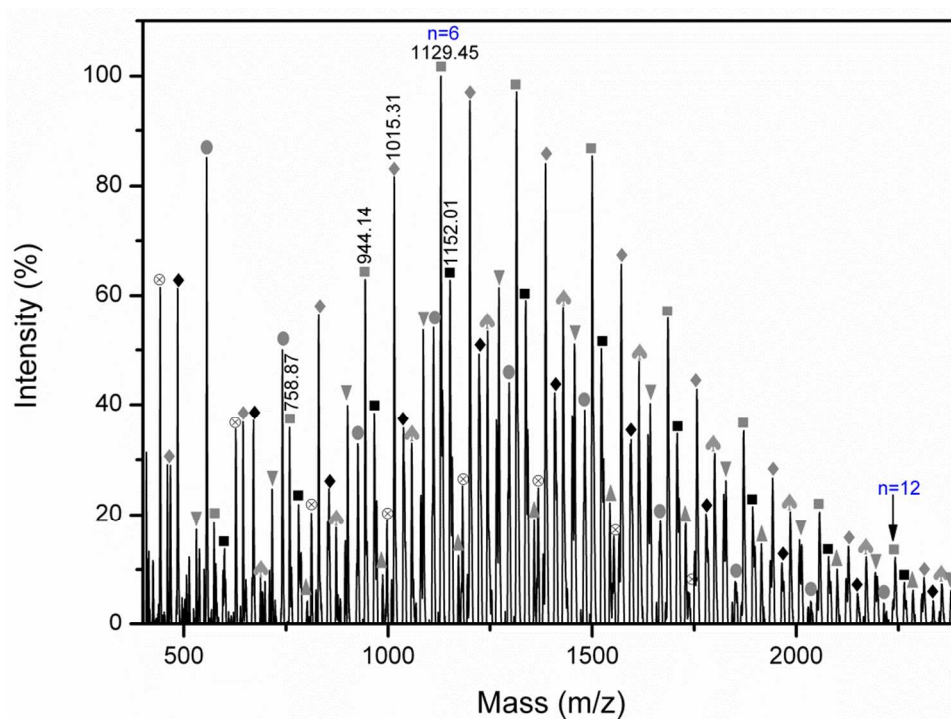
**Table S2.** Structures list of the symbols for figure S8 and figure S9

Symbol adduct	Structures	Mass of end group (amu)
$H^+$ :  $Na^+$ : 		18
$H^+$ : 		0
$H^+$ : 		71
$H^+$ :  $Na^+$ : 		89
$H^+$ :  $Na^+$ : 		160
$H^+$ :  $Na^+$ : 		231.1
$H^+$ : 		302.2
$H^+$ : 		132.1
$H^+$ : 		246.1

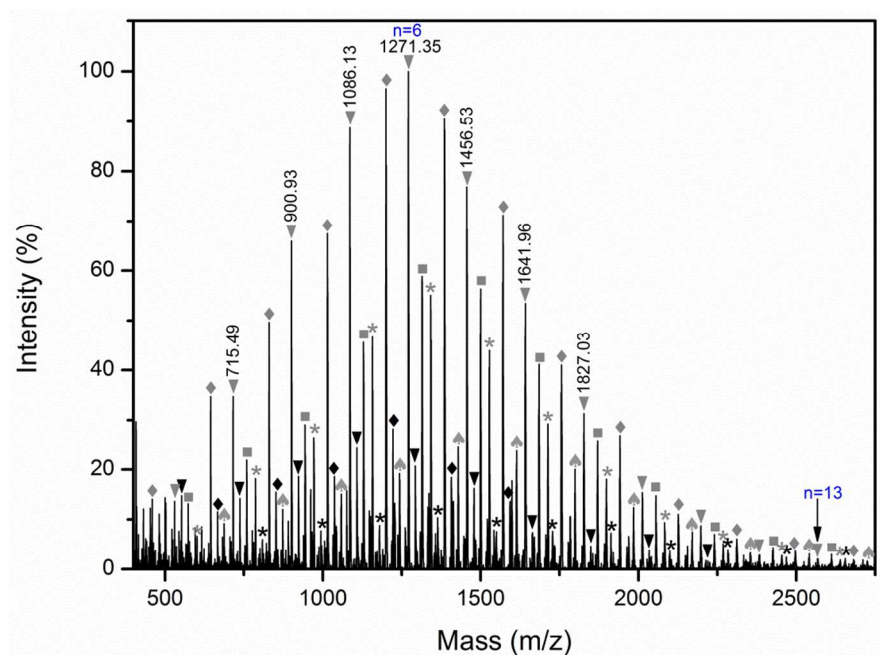




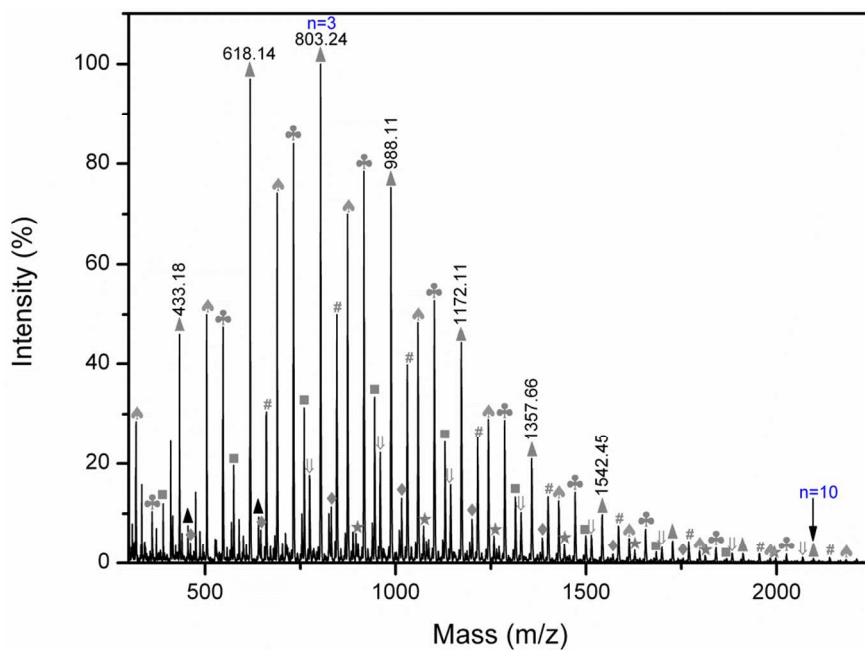
**Figure S7.** MALDI-ToF spectrum of the side product dissolved in formic acid



**Figure S8.** MALDI-ToF spectrum of poly( $\epsilon$ -CL-*co*- $\beta$ -lactam) with addition of NaTFA


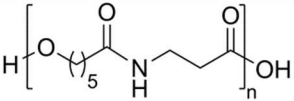

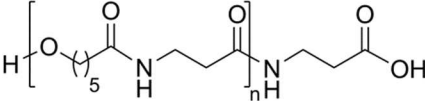


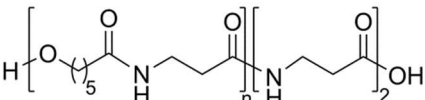

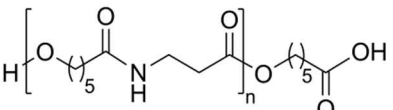


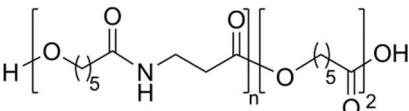

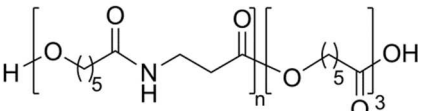

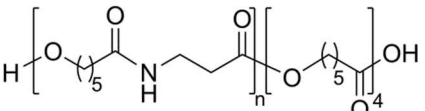

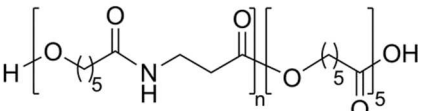

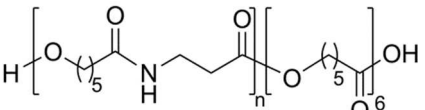


**Figure S9.** MALDI-ToF spectrum of poly( $\epsilon$ -CL-*co*- $\beta$ -lactam) from the reaction with feed ratio 75:25 of  $\beta$ -lactam: $\epsilon$ -CL

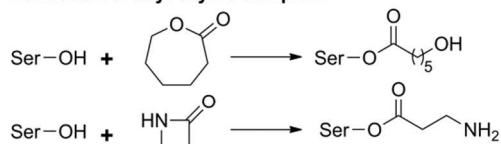


**Figure S10.** MALDI-ToF spectrum of poly( $\epsilon$ -CL-*co*- $\beta$ -lactam) from the reaction with feed ratio 25:75 of  $\beta$ -lactam: $\epsilon$ -CL

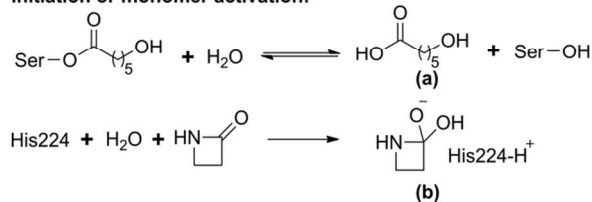
**Table S3.** Structures of poly( $\epsilon$ -CL-*co*- $\beta$ -lactam) from the reaction with feed ratio 25:75 of  $\beta$ -lactam: $\epsilon$ -CL

Symbol adduct	Structures	Mass of end group (amu)
$H^+$ : 		18
$H^+$ : 		89
$H^+$ :  $Na^+$ : 		160
$H^+$ : 		132.1
$H^+$ :  $Na^+$ : 		246.1
$H^+$ : 		360.2
$H^+$ : 		474.2
$H^+$ : 		588.3
$H^+$ : 		702.4

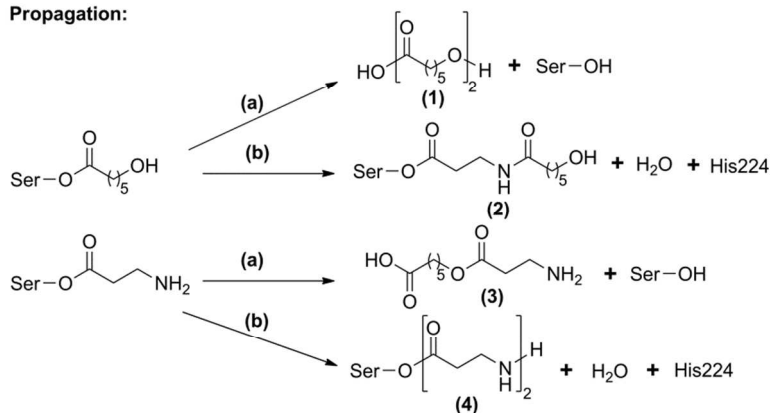
**Formation of acyl-enzyme complex:**



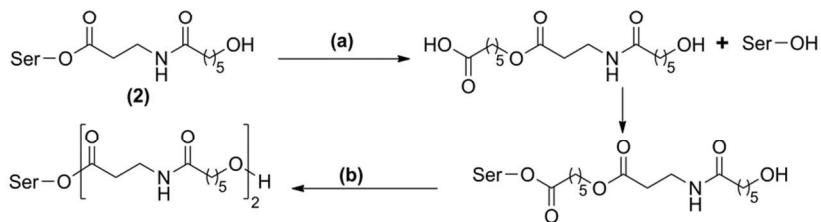
**Initiation or monomer activation:**



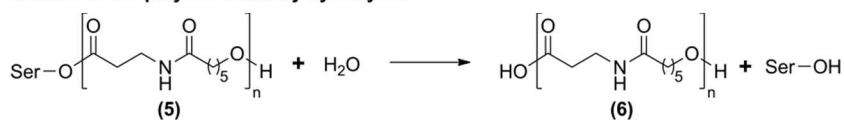
**Propagation:**



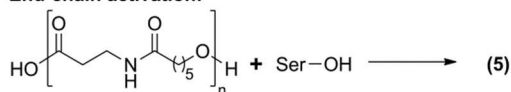
**Formation of alternating copolymer:**



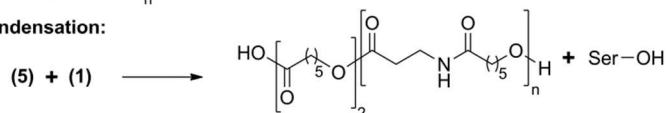
**Release of the polymer chain by hydrolysis:**



**End-chain activation:**



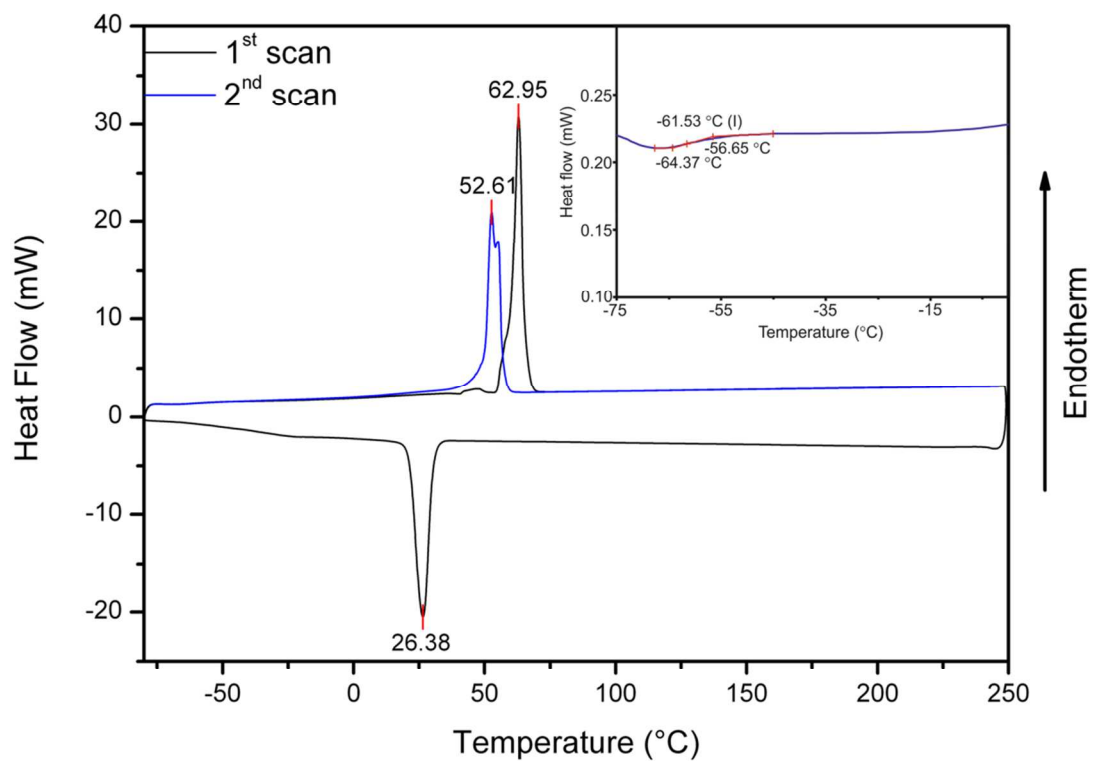
**Polycondensation:**



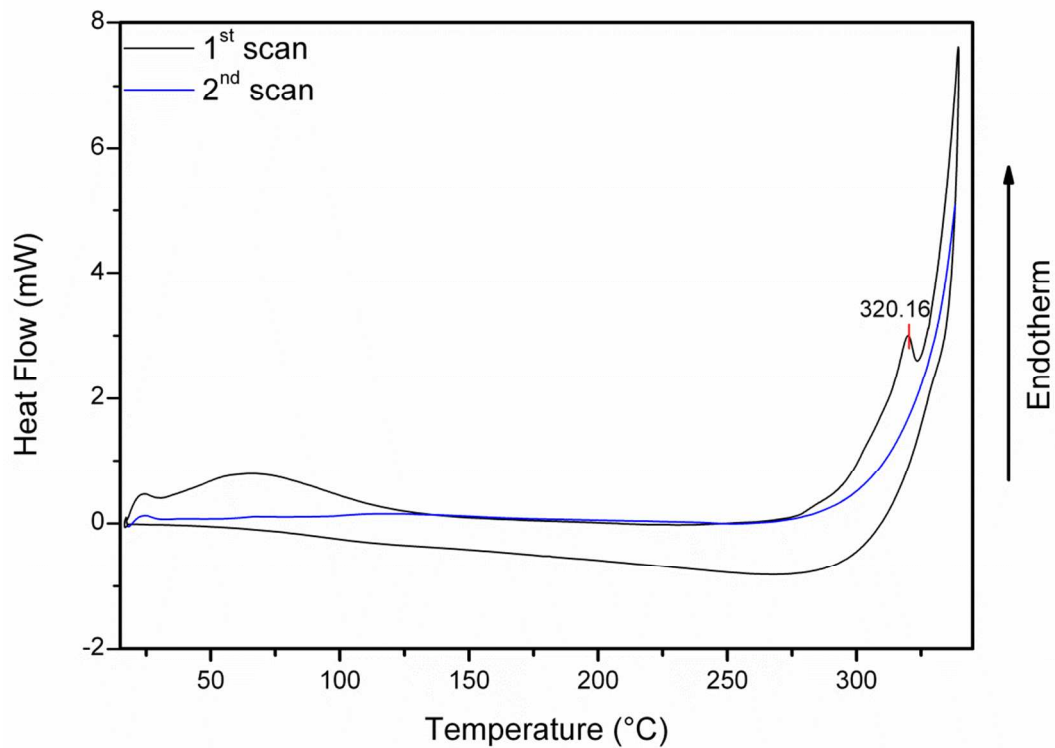
**Intra-chain activation of oligo( $\epsilon$ -CL):**



**Scheme S1.** Proposed reaction mechanism of CAL-B-catalyzed formation of poly( $\epsilon$ -CL-*co*- $\beta$ -lactam).



**Figure S11.** DSC curves of poly( $\epsilon$ -caprolactone)



**Figure S12.** DSC curves of poly( $\beta$ -lactam)